

subcutaneous group. We conclude that subcutaneous administration of alemtuzumab shows similar outcomes as intravenous administration in the reduced intensity preparatory regime for non-malignant diseases with less toxicity to the patient.

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USE OF A CALCIUM/PHOSPHATE ORAL RINSE (CAPHOSOL[®]) TO LESSEN THE MUCOSITIS FOLLOWING AUTOLOGOUS PERIPHERAL BLOOD STEM CELL TRANSPLANTATION

Bechtel, T.P.¹, Devine, S.² ¹Arthur G James Cancer Hospital and Richard J Solove Research Institute at the Ohio State University Medical Center, Columbus, OH; ²Arthur G James Cancer Hospital and Richard J Solove Research Institute at the Ohio State University Medical Center, Columbus, OH

The high-dose chemotherapy/radiation therapy employed in the conditioning regimens prior to hematopoietic stem cell transplantation have a considerable negative effect on the oral epithelium. Depending on the agents and doses administered, oral mucositis can range from mild to life threatening. The consequences of this mucositis, depending on its degree, can impact a patient's ability to maintain oral hydration, nutrition and intake of medications. Additionally, the potential for local and systemic infections increases dramatically with the loss of the natural mucosal barrier. Many interventions have been tried over the years to lessen the degree of mucositis and all have met with mixed, inconsistent results. The recent introduction of a new agent, Caphosol[®], has added to the list of potential treatments. One conditioning protocol that has consistently produced varying degrees of mucositis in our patients is the BEAM regimen. It consists of carmustine, etoposide, cytarabine and melphalan given intravenously over a 6 day period and is widely used in the non-Hodgkins lymphoma population. Previous attempts to modify the mucositis have been met with marginal success so it was decided to trial Caphosol[®] in this setting. Caphosol[®] was prepared according to the manufacturers instructions and administered 4 times daily to 9 patients receiving the BEAM regimen. This group was compared to 13 patients that received BEAM in the previous 6 months who did not get Caphosol[®]. Some degree of mucositis was seen in all the patients which required narcotic analgesic intervention. The most severe cases required the use of patient controlled analgesia (PCA) with either morphine or hydromorphone. We found that four (4) patients in each group needed PCA however the Caphosol[®] group needed a mean of only 4.25 days of PCA therapy vs 5.5 days in the other group and the overall patient pain rating was less in the Caphosol[®] population. We also found that the length of stay after transplantation (LOS) was 1.5 days less in the Caphosol[®] group (14.5 vs 15.9 days) while the mean number of days on Caphosol[®] was 10.2. It was felt that the treatment had a positive effect on patient outcome and quality of life and it is now used in all patients receiving BEAM therapy. We continue to evaluate it in this group along with other transplant populations, non-transplant chemotherapy patients and those receiving radiotherapy for head/neck cancer.

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ATTENUATED KERATINOCYTE GROWTH FACTOR AND ETOPOSIDE BASED CONDITIONING FOR ALLOGENEIC TRANSPLANT

Booth, D.L. Royal Melbourne Hospital, Melbourne, Victoria, Australia

Objective: Assess the impact of keratinocyte growth factor (KGF) administered prior to conditioning only, on oral mucositis in allogeneic transplant recipients receiving etoposide based conditioning.

Method: All patients scheduled for HSCT with TBI/ Etoposide or Bu/Cy/Etoposide from June 2006 to August 2008 were offered KGF at 60 mcg/kg on 3 consecutive days finishing 24 hours prior to conditioning. Work previously done in our institution showed KGF was not beneficial in allogeneic patients receiving myeloablative conditioning regimens. This result was attributed to scheduling of post conditioning KGF and short course methotrexate despite omission of day +1 KGF to avoid coadministration within 24 hours. Therefore, in this cohort of patients post conditioning KGF doses were omitted completely. WHO oral mucositis score, duration, TPN and analgesia usage were recorded prospectively.

Results: Twelve patients (8 allogeneic, 4 MUDs, 7 B-ALL, 2 Ph+ve ALL, 2 T-ALL, 1 biphenotypic leukaemia) consented to

KGF. Conditioning was TBI/etoposide in 10 patients TBI/thymoglobulin/etoposide in 1 patient and Bu/Cy/etoposide in 1 patient with CSA and MTX on days 1, 3, 6 and 11 as GVHD prophylaxis. Grade 3 to 4 mucositis was experienced by 8/12 patients (67%) compared to 36/38 (95%) of TBI etoposide patients prior to June 2006 (P = 0.024). Mean duration of TPN was 13.5 days compared to 18 days and mean duration of opiate analgesia was 11.5 days compared 14.5 days for KGF cohort and the historical cohort respectively.

Conclusions: Attenuated KGF is effective for amelioration of oral mucositis associated with etoposide containing conditioning in allogeneic transplants.

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A RAPID NANOPARTICLE IMMUNOASSAY TO QUANTITATE BUSULFAN IN PLASMA

Salamone, S.J.¹, Benfield, C.N.¹, Courtney, J.B.¹, Harney, R.L.¹, Kozo, D.R.¹, Li, Y.¹, Lundell, G.D.¹, Shaw, L.M.², Gardiner, J.A.M.² ¹Saladax Biomedical Inc, Bethlehem, PA; ²University of Pennsylvania Medical Center, Philadelphia, PA

Background: Busulfan (BU), a bifunctional alkylating agent, is the most widely used chemotherapeutic agent as a component of high-dose conditioning regimens for hematopoietic stem cell transplantation (HSCT). Studies have shown that maintaining a targeted exposure [expressed as area under the time-curve (AUC)] throughout the complete regimen is essential for successful engraftment, reduced risk of graft vs. host disease or venoocclusive disease. For optimal therapeutic drug management (TDM), an assay that can deliver rapid high quality results would be desirable.

Methods: Monoclonal antibodies bound to nanoparticles were used to develop an immunoassay for the Roche c111 chemistry analyzer. The assay was monitored at 629 nm and quantitated with a stabilized calibrator of busulfan. Assay precision, linearity, calibration stability and limit of detection (LoD) were determined. Clinical samples were analyzed and correlated with GC-MS.

Results: With six calibrators from 0–2,000 ng/mL, a stabilized busulfan derivative, and auto-dilution, plasma samples with concentrations up to 10,000 ng/mL could be determined. Time-to-first-result was 12 min and 25 samples/h could be measured from a stored standard curve. Imprecision across the range of assay was <7% and the assay was linear upon dilution over the entire range. Cross-reactivities for sulfolane, tetrathiothiophene and 3-hydroxysulfolane were <1%. The LoD was 50 ng/mL with a functional sensitivity of 100 ng/mL. Assay results of clinical samples (237 to 1,711 ng/mL) correlated well with GC-MS results: (R > 0.98, slope 1.05, intercept = 39 ng/mL).

Conclusions: This immunoassay is suitable for determining busulfan concentrations in plasma. It offers advantages of turn-around time, small sample size, no sample pre-treatment and a stable calibrator that can be stored at room temperature. Automation and rapid turn-around time with a small benchtop analyzer enable efficient routine monitoring of busulfan concentrations in clinical practice which can lead to better patient care.

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PHARMACOKINETIC (PK) COMPARISON OF INTRAVENOUS VERSUS ORAL BUSULFAN CONDITIONING REGIMENS FOR ACUTE MYELOID LEUKEMIA (AML) AND MYELODYSPLASTIC SYNDROME (MDS) PATIENTS

Hutcherson, D.A.¹, Surati, M.¹, Sanvidge, K.¹, Harvey, D.², Al-Baldawi, R.N.³, Langston, A.², Flowers, C.², Lonial, S.², Kaufman, J.², Lechowicz, M.J.², Waller, E.² ¹Emory Healthcare, Atlanta, GA; ²Emory University, Atlanta, GA; ³Mercer University, Atlanta, GA

Background: Busulfan (Bu) and cyclophosphamide are widely used in conditioning regimens before hematopoietic cell transplantation. Increased relapse rates and graft rejection have previously been reported with low Bu area-under-the-curve (AUC) micromol*min/L, and sinusoidal obstruction syndrome is associated with high AUCs. This has led to strategies to adjust Bu dosing to achieve a target AUC. Previous studies have suggested that a 0.8 mg/kg dose of IV Bu would achieve an AUC similar to that of 1 mg/kg of oral Bu. PK monitoring of IV Bu at our institution demonstrated that